Henry Ford Hospital Medical Bulletin

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Abstracts of all recent papers will be published, in so far as possible, as well as scientific articles and addresses by the Professional Staff.

HENRY FORD HOSPITAL
MEDICAL BULLETIN

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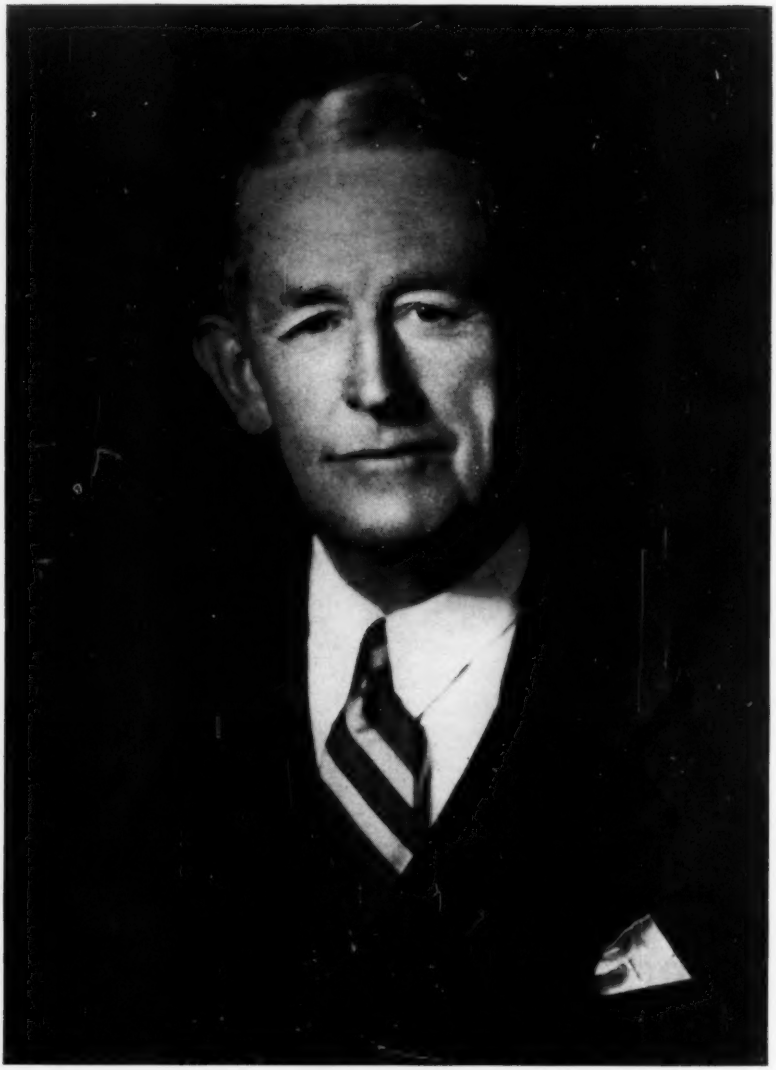

DR. FRANK J. SLADEN

This photograph of Dr. Sladen is published with thanks for his many years of scholarly instruction, devoted leadership and personal inspiration.

The Professional Staff

Dr. FRANK J. SLADEN

The career of Dr. Frank J. Sladen might be expressed as concerned with four periods of activity. The first, that of training and preparation amounted to eleven years at The Johns Hopkins Hospital and abroad as a member of the Hospital staff and of the Medical School Faculty. The second had to do with the beginnings and development of the Henry Ford Hospital; the third, the War Service; and fourthly the administrative and executive functions in the conduct of the Department of Medicine and of the now mature phase of our Hospital.

It is possible to refer here only briefly to a number of his contributions. Noteworthy is the work on the then little known process of the coagulation of the blood with Frank Hinman, in medical student days.[1] The responsibility for the study and application of antimeningitis serum (Flexner) a product of Dr. Simon Flexner, Director of The Rockefeller Institute, resulted in a number of reports.[2] The 66% mortality of meningococcus infections prevalent at the time was reversed to a 75% recovery. During this period, he reported with Dr. Harvey Cushing the first instance of the application of therapeutic serum by the cerebral intraventricular route.[3] Studies of the autonomic nervous system and of the pharmacodynamic reactions, just introduced by Slesinger of Vienna followed, with Dr. Lewellys F. Barker.[4]

For twenty years the basic factors of individual personal health have occupied his interest leading to such developments as studies of the longitudinal curve of life and of the constitutional background of chronic diseases, particularly as applied to rheumatoid arthritis and degenerative states.

In 1940 he delivered the address of dedication of The Physician's Window at the National Cathedral, Washington, D. C. A major interest in bridging the gap between religion and medicine has been carried out for several years under the National Council of Churches. His organization and conduct of the National Conference on Psychiatry and the War in 1942 must be noted. Dr. Sladen was the editor of a volume under that title published by Charles C. Thomas.[5] Several publications have appeared over his name giving intimate pictures of Sir William Osler and his bedside and clinic teaching. Dr. Sladen's interests at the present time are concerned with the largely unexplored field of the problems of the aging population and with the basic factors in the so-called physiological aging process of man.

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THE DIGNITY OF THE PRACTICE OF GENERAL MEDICINE*

FRANK J. SLADEN, M.D.

Physician-in-Chief 1915-1952

Consultant to the Medical Service

Henry Ford Hospital

In addressing you today, I realize I have the honor of giving the Roy D. McClure lecture, by your invitation.

I have chosen as the subject THE DIGNITY OF THE PRACTICE OF GENERAL MEDICINE because I believe it is timely and pertinent and a very important subject for our consideration together.

By the scientific method of advance we are said to move from facts to generalizations, from generalizations to greater generalizations.

The practice of general medicine is described by authorities to have been early interpreted as general in scope and not confined to a specialty. Call it General Practice if you wish. They are synonymous. I prefer the term "the Practice of General Medicine" because it seems to open more possibilities for training and skill and is more likely to receive the recognition deserved for services rendered.

After the same education and training, the majority, if not all, of the graduating class in medicine is prepared and ready for the practice of General Medicine.

This was the situation with Dr. McClure in 1908, when, at the age of 26, he had completed his college work at Ohio State University and his medical work at Johns Hopkins. Born of a doctor father who himself practiced General Medicine in Columbus, Ohio, his preparation for his life work was carefully planned.

During the school years he studied abroad at the University of Prague in Bohemia and spent a year at the Rockefeller Institute in research with the famed Dr. Alexis Carrel before becoming a house officer in surgery at the New York Hospital.

In 1912 he returned to the Johns Hopkins Hospital where he completed his training in surgery serving five years under Dr. William S. Halsted. He wrote an excellent account of the Halsted School of Surgery. Dr. Halsted was his source of inspiration and influenced him tremendously in his method of training younger surgeons and in many other ways.

At the time of his death, March 31, 1951, he had served exactly 35 years, almost to a day, as Surgeon-in-Chief of the Henry Ford Hospital, and had been a

*The Roy D. McClure lecture. Given before the Michigan Academy of General Practice and the American Academy of General Practice of Wayne County, November 8, 1951.

Trustee of the institution since 1938. His leadership here and his contributions to the building of this institution and its principles and practices are beyond enumeration. His publications began in the third year of his medical schooling and continued, 117 in number, to include three papers published since his death.

Dr. McClure is gone but much of him lives in this institution and in this generation. We feel a real sense of warmth in acknowledging his continued participation in our work and our planning here now day by day.

I was thinking of a volume I have, entitled ESCAPE FROM OBLIVION. What will be remembered the longest, of Dr. McClure? Will it be his skill as a surgeon? His interest in teaching? His accomplishments in research? Or Dr. McClure as a man? His personality, his outgiving nature, his gentle kindliness? His friendliness, mixed always with dignity and reserve on a base of Scotch determination and perseverance to see through to the end what he felt was right?

The term GENERAL MEDICINE may be interpreted as having a different connotation by others, but originally it included the wide field of medical practice, as it implies. It is not true historically that all the specialties grew out of it, but most of them did. Nevertheless, it is generally admitted that a thorough training in general medicine provides the best, broad base upon which devotion to a smaller, special field can be founded.

I believe the practice of general medicine is in the process of being elevated to as high and skillful a standard as any field of medicine. That recent leaflet of the American Medical Association entitled A DOCTOR FOR YOU lays the foundations excellently. In quoting it runs, "America's M.D.'s are . . . interested . . . in seeing that you have a capable, understanding physician." Dr. Lester D. Bibler, addressing the Indianapolis Torch Club, said, "I believe that every family should have a family doctor, one whom they may feel free to consult with every type of illness. It is the aim of the American Academy of General Practice that all such family doctors shall be alert, well-trained, and qualified for the medical and surgical care that they are to perform."

The answer to future medical care is said to be in what actually is adequate medical care.

There is, I believe, something consistent with this picture in the expression "the practice of general medicine" in preference to the customary reference to "general practice."

At any rate, with the swing of the pendulum back again we must recognize that special training for the practice of general medicine must be provided. We feel so strongly that this field forms a necessary basic training for everyone, that we have established four medical clinics for the practice of general medicine and the training of younger men in the field of general medicine, in this hospital.

Perhaps you saw in the New York Times of October 28th a notice of the meeting of the New York State Academy of General Practice. Dr. Samuel A. Garlan,

the President, said, "the Academy was organized to challenge the position of medical over-specialization and to interest the American public in the family doctor as a family counselor. About 95% of all routine medical problems can be handled," he said, "by a qualified general practitioner, according to studies of the Academy."

However, the aims of the Michigan Academy printed upon the blue program leaflet provide greater appeal and better publicity than Dr. Garlan's reported statement.

The best publicity, however, resides in the man himself who does everything within his power to keep abreast of the rapidly changing medicine of the day and attempts to bring to the benefit of his patients what he conscientiously believes is best for them.

Dr. Hamilton W. McKay in his presidential address to the Southern Medical Association stated, "We know that it is true that more people get better medical care today in America than in any other country in the world. We know that we have a program of medical education second to none. We know that we have a system of hospitals, clinics, and medical centers, small and large, that is the envy of the whole world."

"But the trouble with most of us is that we stop our thinking right there." He then points out that our fellow citizens are judging us not in these terms but against the standards of American demands.

Quoting him further, "We are being weighed against the balance of strictly American standards. Our public relations are being weighed against the public relations standards which Americans have come to respect in other pursuits. Our competence is being weighed against the standards of competence in other professions. Our charges are being weighed against budgetary demands of other services which are essential to life and happiness in America."

Continuing to quote him, "The primary purpose of this discussion is to make it as clear as I possibly can that ultimate responsibility for the freedom and welfare of American medicine rests squarely upon the individual doctor and his friends in related organizations in the field of general medicine."

"Above all else, it means that liberty is possessed only by those who earn the right to be free and employ that freedom in such a fashion as to maintain and enhance the respect and confidence in which the physician is held in his community."

Forced by the limitations of time, one might express this in these few words. The medical profession is said to be challenged by the need of exploring a "new frontier of science," namely, the attitude of the public toward medicine as it is practiced, public relations, the relations of the public to the medical profession. This is based primarily upon us of the profession and our relations to the public.

Edmund W. Sinnott, dean of the scientific school at Yale, says, "the scientist is the spiritual descendent of the old explorers." This is in an article entitled

"The Frontiers of Science." After referring to the explorations of the universe around us, of the atmosphere about the earth and what is as yet unknown about the character of matter, he speaks of the exciting things that are happening along the frontiers of life, of such great significance:

—the frontiers of the viruses, intermediate between organisms and protein molecules;

—the frontiers of heredity and the genes which also seem to be protein molecules;

—the frontiers of the isotopes, now produced so abundantly by the atom smashers and their already proven value in biology and medicine;

—the frontiers of the cell itself, now being unfolded from chaos to an orderly organism, a matter of great importance to the study of cancer;

—the frontiers of the hormones, aroused to a state of extreme interest by the work of Kendall and Hench with cortisone and ACTH.

We could add many more, notably the antibiotics; even the antihistamines and a host of others, perhaps of less general application.

Inasmuch as you and I are to dwell in these frontiers a great deal of the time in the future, it is quite essential we formulate a policy that will guide us and give us and our patients safe conduct over dangerous borders.

This is particularly demanded when we are told enthusiastically that "the progress of science, great as it has been over the past century, is surely but just begun. New discoveries open new fields of work quite unsuspected before. Every addition to knowledge, said a famous philosopher, brings an addition to ignorance. An understanding of ultimate truth is surely in the far, far distance."

Again we must emphasize the unpredictable nature of scientific discoveries, both in the field of their successful, useful application and in the unsuspected side revelations, the "serendipity," a term which you may remember Dr. Cannon, the physiologist, discussed when he gave the Beaumont lecture here many years ago.

With this situation in which we find ourselves in the practice of general medicine, continually faced anew with a wide variation of patients and their demands upon us for service, we are besieged with the aggressive activities of salesmen of new pharmaceutical products. It might be added that we are very busy. We have little of the academic freedom of the University professor and are usually too tired to accomplish much in reading the newer significant literature at night.

One more feature militates against us. There is little opportunity for discussion and contact with colleagues who practice under similar conditions. If there were, we would learn many answers for our patients and much of good medicine, just by the momentum of the associations.

Perhaps many of you in the Academy have already experienced the value of free discussion at frequent, stated intervals in groups of 4, 5 or 6. If you have not had this advantage of a discussion group, you cannot realize how much you

absorb of newer and better medicine and how frequently you find the answers to your problems before you finish stating the problem in a small group. After all, it is only one further subdivision of the local divisions of your American Academy.

Why have I gone into all these things which you already know? Because I felt much could be gained by reversing the scientific method of advance referred to at the onset of this talk, that is from facts to generalizations, from generalizations to greater generalizations.

We have dealt with the greater generalizations in considering the frontiers of science; with lesser generalizations in picturing the predicament of the man who is in the practice of General Medicine.

Now let us deal with the pertinent facts.

1. No branch of medicine should be considered less than any other in standard of work and service to patient. No medical man should tolerate any branch of medicine which is not equal with every other within the limitations of its character.

2. The Practice of General Medicine is an opportunity for developing a field of highly specialized medical work. Its challenges differ greatly for the man in the big city and for the man in the village or small town. The establishment of standard qualifications by the American Academy of General Practice has already claimed for it a point ahead of the present certification boards or American Associations and Colleges which in themselves require little or no individual effort of its members. It is my hope and prediction that you will not only pursue this program but expand it in as many directions as you can.

3. If you persevere and go the way of other such programs, the American Academy of General Practice will one of these days find itself soundly established as a tradition of American medicine. The American College of Physicians persisted many years, to my knowledge, without full and enthusiastic recognition by the internists of the country, or by the longer established American College of Surgeons.

In closing, it would be negligent not to point out two features which add dignity to the Practice of General Medicine. The first is the need of impressing the public, the patient, that diagnosis comes before treatment, and diagnosis cannot be made in a moment. Treatment should be more than meeting symptoms, of course, (though some men have been known to prescribe symptomatic treatment on a quick diagnostic impression). If all men practicing general medicine made the effort, patients would soon learn to put top value on the diagnosis first.

In this same category is the danger involved in using these newer medicinal products which appear almost day by day.

The most scientific scientist has the highest degree of scientific skepticism. He believes nothing until it is proven. The use of gold therapy, of the antibiotics, and the hormones, for instance, was fraught with untold dangers until worked out satisfactorily. We who are entrusted with the welfare of private patients can well afford to wait their use until some time when satisfactory reports appear which enable us to move with safety for our patients.

I know patients demand drugs and procedures they read about. In fact, I fought through relatives and friends for two years to avoid giving cortisone or ACTH to a case of rheumatoid arthritis in the specially dangerous late decade. Still, if one's position is right, the strength of one's judgment is enhanced in value ultimately by this stand. If one can follow that program because we are convinced it is right, one can do it and contribute thereby to the soundness and saneness of the practice of General Medicine.

Finally, I cannot close without confessing to you that I believe the greatest advance of the last five years has been in the emphasis put upon the whole man as a problem of the practice of General Medicine.

"Man, not matter, is the chief problem of the world today."

If man is unable to be "the master of himself, he is but half a man." "Only whole men can save the world today."

The dominance of science today has led to a dangerous state in that the mind of man has outrun his spirit. It is to the throng of reactions, instincts, attitudes and mental patterns which seem so variable and often chaotic and without control, to which we point as forming such an important part of every life,—these experiences which deal with emotions, desires, purposes, values, feelings of beauty and ugliness, of right and wrong, of love and hate.

Has not Selye satisfactorily established these under "unresolved stress and strain" as etiological agents of organic disease?

Although heralded as one of the great advances of recent medicine, it seems to me that for centuries doctors have been conscious of the fact that, in order to serve patients best, something must be known of them as persons. However, a recent publication by one of Detroit's leading psychiatrists stated that "the rediscovery of the patient as a person constitutes an important challenge to American Medicine today."

Dr. Benjamin Rush and his thought in 1809 that disease could result from an overdose of theology; Dr. Oliver Wendell Holmes and his protest against the tendency to ignore personality; Dr. Weir Mitchell who initiated the so-called rest cure; Dr. Lewellys F. Barker, a master genius of this generation in the care of people ill from emotional difficulties; these are just a few of those who featured the total personality in their teaching from the early 19th Century to date.

Shryock writing recently on medicine and social science says "the specialist, by definition, was not primarily interested in the patient as a whole."

Right here may I state that the picture of a patient as a total integrated personality is the central figure in the practice of General Medicine, whether it is a matter of dealing with the emotional component of his peptic ulcer or with his illness based primarily upon the fact that he cannot lift the mortgage on his home. No group has a better opportunity to become the experts in this field than the men in the practice of General Medicine. They have the relationship with the family, the opportunity to know of home, work and other influences, to carry out a program of diagnostic, therapeutic and preventive skill in this field of General Medicine which cannot be surpassed.

PITFALLS IN GASTRO-INTESTINAL DIAGNOSIS

JOHN G. MATEER, M.D.
Physician-in-Chief
Henry Ford Hospital

Introduction

The discussion of pitfalls or errors in diagnosis is a more effective method of improving diagnostic accuracy than focusing attention upon the achievements of various diagnostic procedures. Diagnostic errors should be and usually are invaluable although painful stepping stones to real and lasting progress.

Frequently, misdirected treatment, both medical and surgical, in the field of gastro-enterology is due to the incorrect interpretation of gastro-intestinal symptoms and attributing them to the wrong underlying condition. This occurs especially where several underlying abnormalities exist, as so often occurs in the gastro-intestinal tract.

Confused thinking usually can be avoided if one makes the classical three-fold anatomical, functional and etiological diagnosis, outlining clearly in one's mind the evidence for each. The functional diagnosis should attribute the several symptoms to the correct underlying cause or causes. If the ultimate etiology of each of the several conditions is not known, it is essential at least to clarify in one's mind the important contributing or aggravating factors. The therapeutic emphasis will then be directed toward the correct underlying condition or conditions and from an etiological approach. To evaluate the functional diagnosis correctly, it is necessary to know the various differential points in the symptomatology of the several underlying conditions.

It seems worth while to summarize briefly, without going into unnecessary details, those errors in gastro-intestinal diagnosis which are made from time to time and may lead to unfortunate and sometimes disastrous results. These errors are not made as often as they were made twenty years ago, but they still occur more often than they should. They may be summarized concisely in outlined form as follows:

I. *Confusion Between Gallbladder and Chronic Irritable Colon Pain and Tenderness*

Failure to interpret correctly right upper quadrant pain and tenderness may lead to cholecystectomy for relief of colon pain. This error is due to failure to appreciate (1) the several characteristics of irritable colon distress, (2) the importance of examining such patients in the sitting position in order to identify true gallbladder or liver tenderness and differentiate it from irritable colon tenderness and (3) the fact that chronic irritable colon is a much more common cause

of right upper quadrant pain and tenderness than chronic inflammation of the wall of the gallbladder or gallstone colic.

Often it is wise to advise cholecystectomy to prevent complications of cholelithiasis in patients whose right upper quadrant pain is on a colon basis; but such patients should be told in advance that cholecystectomy probably will not relieve their colon pain.

II. *Errors in Intestinal Diagnosis*

1. The assumption is often made that the association of amoebiasis with colon distress means that the colon distress is due to amoebiasis, whereas 65% of the cases of amoeba histolytica infestation are latent and do not cause symptoms. Patients whose stools no longer reveal amoebae frequently receive unnecessary repeated courses of amoebicidal drugs for relief of persistent colon distress. Such cases usually are not actually relieved of their distress until they receive irritable colon therapy.

2. Many cases of latent amebiasis are not found because warm stools are not examined routinely.

3. Numerous cases of early, atypical, non-tropical sprue are misdiagnosed as chronic irritable colon. The fairly frequent occurrence of sprue is not always appreciated and often sprue is not even considered in differential diagnosis when it should be. In such cases, therefore, there is a failure to conduct the oral glucose tolerance test, stool studies for unabsorbed fat and roentgen-ray studies of the small intestine.

4. Rectal polyps, which are frequent precursors of rectal carcinoma, are often overlooked and not removed because proctoscopic examinations are not done frequently enough.

5. Rectal and colonic cancer are still missed because rectal bleeding is not always considered as an indication for a proctoscopic examination and barium enema.

6. Early carcinoma of the distal colon, with recent constipation as the only symptom, still may be treated temporarily only for constipation, because a barium enema is not obtained always before treating constipation as a symptom.

7. Diagnosis of regional ileitis is often missed because x-ray studies of the small intestine often are not conducted when they should be.

8. Fortunately, the fallacious clinical diagnosis of chronic appendicitis, as a cause of symptoms, has waned.

III. *Misinterpretation of Liver Function Tests*

1. The degree of functional hepatic impairment may be interpreted incorrectly as indicating a corresponding degree of organic impairment.

(a) In acute hepatitis impairment of liver function and structure do tend to run rather parallel.

(b) In chronic liver disease there is often considerable dissociation of impaired function and structure. Some cases with moderately well-developed cirrhosis may exhibit only slight impairment of function. Conversely, certain cases with only slight organic impairment, as indicated by liver biopsy, may show rather marked functional impairment.

(c) Therefore, if comprehensive as well as accurate information about the liver is desired, both liver function tests and liver biopsy studies are indicated.

2. A second common error in interpreting liver function tests occurs in jaundiced patients and consists of drawing the same deductions from the results of function tests in patients with early and late jaundice. In late jaundice the usual interpretation of these tests is unreliable for obvious reasons.

IV. *Causes of Errors in Differentiating "Medical" and "Surgical" Jaundice*

1. Failure to observe and study jaundiced patients for at least 7-10 days, or longer, if there is any disagreement between diagnostic data, before attempting to make a final diagnosis.

2. Failure to appreciate that complete suppression of bile flow in acute hepatitis occasionally persists for 10-14 days, instead of only 2-3 days. This may mislead one into an incorrect diagnosis of obstructive jaundice.

3. Failure to appreciate that a painstaking history and physical examination lead to a correct diagnosis in more than half of the cases.

4. Failure to emphasize sufficiently the direct type of laboratory evidence for bile duct obstruction, namely,

(a) repeated chemical examination of the stools for bile and blood,

(b) quantitative urinary urobilinogen test and (c) the blood prothrombin determination before and after parenteral vitamin K. administration.

5. Failure to interpret the indirect laboratory evidence from other liver function tests in relation to the duration of the jaundice.

6. Failure to search for primary carcinoma elsewhere in the body as a source for possible metastatic carcinoma in the liver.

7. Problem of differentiating the two types of obstructive jaundice, (intrahepatic and extrahepatic).

(a) Chronic cholangiolytic hepatitis tends toward more or less normal liver function with associated complete and persistent intrahepatic obstruction to the bile flow. It may be extremely difficult or impossible to differentiate it from extrahepatic obstruction of the common bile duct. Fortunately, no harm is done by exploring patients with the cholangiolytic type of hepatitis, since liver function as a rule is essentially normal.

V. *Erroneous Diagnosis of Duodenal Ulcer*

1. Functional pylorospasm may be diagnosed as a duodenal ulcer.

2. This error can be avoided by a painstaking history and a critical interpretation of x-ray findings.

3. The eight characteristics of peptic ulcer distress, which if present differentiate it from pylorospasm and other types of epigastric distress, should be inquired for in every patient with epigastric distress.

4. A typical ulcer history indicates the presence of a peptic ulcer. An atypical history throws grave doubt on the diagnosis of ulcer, although a small per cent of patients with ulcer complications yield a somewhat atypical history.

5. A probable clinical diagnosis of active ulcer or no ulcer should be made in every suspected case, since the x-ray examination often does not portray an ulcer crater as direct evidence of an active ulcer even when an ulcer exists. The more frequently found, generalized x-ray deformity of the duodenal bulb indicates either a present or previous ulcer.

VI. *Fatal Error of Diagnosis of a Malignant Gastric Ulcer as Benign, with Prolonged Medical Treatment*

1. Initial history and x-ray studies of malignant ulcer may simulate benign ulcer.

2. The three classical points of differential diagnosis, namely, the prompt disappearance under therapy of the distress, the x-ray defect and the occult blood from stools in benign gastric ulcer have value, but also distinct limitations.

3. Repeated follow-up x-ray and gastroscopic examinations during treatment over a considerable period are absolutely essential in medical treatment of gastric ulcer.

4. Even the complete growth of epithelium over a healing gastric ulcer, gastroscopically noted, does not rule out a malignant type of ulcer, with subsequent recurrence of ulceration in this location.

5. The only way to avoid the above serious diagnostic error is to advise surgery promptly, if there is *any suggestion* of malignancy either in the original or follow-up studies and observation.

VII. *Problem of Determining the Cause of Hematemesis*

1. Oesophageal varices of hepatic cirrhosis, as the probable cause of hematemesis, are suggested if one can demonstrate either (a) clinical evidence of cirrhosis, (b) appreciable retention of bromsulfalein dye, or (c) a reduction of the serum albumen. Bleeding from varices is usually profuse and at times fatal.

2. Bleeding from a *chronic* peptic ulcer is suggested if a history of previous ulcer-like distress or of previous x-ray evidence of an ulcer is obtained.

3. Bleeding from an *acute* peptic ulcer is suggested if none of the findings noted above under (1) or (2) are present.

4. Hypertrophic gastritis occasionally causes hematemesis, as has been demonstrated gastroscopically. (Unless this latter examination is conducted, bleeding from hypertrophic gastritis cannot be differentiated from that of a single, acute peptic ulcer.)

5. The more rare causes of hematemesis will not be discussed here.

VIII. *Confusing Perforated Duodenal Ulcer with Acute Pancreatitis*

1. Both conditions present severe epigastric pain and protective muscle spasm, with fever and leukocytosis.

2. History of previous ulcer-like distress and previous x-ray evidence of ulcer, if present, and the demonstration by x-ray of free air in the peritoneal cavity make the diagnosis of perforated ulcer in such cases.

3. Presence of elevated blood diastase and absence of any of above evidence of ulcer point to acute pancreatitis in cases of this type.

4. Prompt operation is essential for perforated ulcer, whereas our statistics show that most cases of acute pancreatitis progress better without surgery.

5. If occasionally early differential diagnosis is impossible, prompt laparotomy is indicated for obvious reasons.

IX. *Causes of Failure to Make Relatively Early Diagnosis of Primary Carcinoma of Stomach*

1. Failure of symptoms to appear early.

2. Failure of patient to consult physician when symptoms first appear.

3. Failure of physician in some instances to obtain repeated stool examinations for occult blood and *repeated* follow-up roentgen-ray examinations of stomach in all patients with recent onset of epigastric distress.

4. Failure to conduct a gastroscopic examination when other studies yield negative results in such cases.

The above array of pitfalls and possible errors in diagnosis is not intended to detract in any way from the remarkable progress made by the medical profession in recent years in advancing the accuracy of medical diagnosis, nor to imply that the above errors are made frequently. Rather, it is hoped that the above comments simply may call attention to those areas of gastro-intestinal diagnosis where one should stop, look and listen.

INHALATION AND NASAL INSTILLATION OF CRYSTALLINE B12 THERAPY IN PERNICIOUS ANEMIA

RAYMOND W. MONTO, M.D.*
JOHN W. REBUCK, M.D., Ph.D.**
MICHAEL J. BRENNAN, M.D.***

Parenteral therapy of pernicious anemia with vitamin B_{12} has been established as the treatment of choice while oral administration of the drug has been ineffective except in massive doses or in combination with "intrinsic factor."[1,2,3] In view of the demonstration that pharmacologic agents may be absorbed from the respiratory tract mucosa[4], this report is a summary of one year's experience with crystalline B_{12} inhalation and nasal instillation in the treatment of pernicious anemia.

METHODS AND MATERIALS

Six cases of pernicious anemia in relapse were treated with vitamin B_{12} by inhalation or nasal instillation. Three of these patients received crystalline B_{12} in physiological saline without a preservative by vaponephrin nebulizer. B_{12} lactose powder was administered to one patient by dust inhalator (aerohalor—Abbott). Nasal instillation of vitamin B_{12} in saline was utilized in the last two cases. Twenty patients with pernicious anemia in remission were given inhalation B_{12} therapy at comparable intervals to maintenance parenteral treatment.

CASE REPORTS

Case 1. F.Z., a white male, aged 56 years, presented classical clinical and hematological findings of pernicious anemia with an initial erythrocyte count of 1,360,000. On the 8th day of B_{12} aerosol therapy a maximum reticulocyte response of 44.2% was obtained. The subsequent treatment and course of the patient are shown in Chart 1. The bone marrow and peripheral blood smears before and three weeks after therapy are illustrated in Figure 1.

Case 2. L.H., a white female, aged 71 years, was studied for mild manifestations of pernicious anemia and minimal peripheral neuritis. Her response to therapy is depicted in Chart 2.

Case 3. S.G., a white female, aged 51 years, demonstrated typical manifestations of pernicious anemia with an initial erythrocyte count of 1,640,000.

*Chief of Division of Hematology.
**Associate in Department of Laboratories.
***Formerly Associate in Division of Hematology. Now serving in U. S. A. M. C.

Treatment consisted of inhalation of B_{12} lactose powder which resulted in the production of over 400,000 erythrocytes a week in the first twenty-one days of therapy, Chart 3.

Case 4. C.C., a white male, aged 66 years, with usual findings of pernicious anemia did not respond to oral administration of B_{12} (15 mcg. daily) for 10 days, but demonstrated a satisfactory course on inhalation at the same dose, Chart 4.

Case 5. J.P., aged 82 years, white male with severe pernicious anemia in relapse was given a single inhalation of 100 mcg. crystalline B_{12} followed by a reticulocytosis of 17% on the 5th day. Three weeks after his initial therapy nasal instillations were administered daily with the hematological improvement shown in Chart 5.

Case 6. J.A., white male, aged 69 years, with classical findings of pernicious anemia of a moderate degree (erythrocytes 2,880,000) was treated by a single nasal instillation of 100 mcg. of B_{12} in 1 ml. saline. On the 8th day a reticulocytosis of 37% was recorded. Three weeks later reinstitution of nasal therapy resulted in continued satisfactory improvement, Chart 6.

The twenty patients on maintenance inhalation therapy for one year have had no evidence of relapse and appear to be adequately treated.

DISCUSSION

The six cases presented in this paper demonstrate the efficacy of the treatment of pernicious anemia by inhalation and nasal instillation of crystalline vitamin B_{12}. Further, the maintenance of pernicious anemia in remission by inhalation B_{12} therapy has proved feasible. Inhalation and nasal instillation of crystalline vitamin B_{12} in saline and lactose powder has thus far produced no irritating or sensitizing action at the local sites.

Oral administration of vitamin B_{12} in amounts of 10,000 mcg. results in urinary excretion of less than 0.05 millimicrograms per ml. On the other hand, inhalation of 200 mcg. of B_{12} in saline produced an urinary excretion of 0.26 millimicrograms per ml. Direct instillation of 100 mcg. of B_{12} into the pulmonary tree by means of a bronchoscope gave an urinary excretion level of 9.76 millimicrograms per ml. Nasal instillation of 200 mcg. B_{12} in saline resulted in a concentration of 1.36 millimicrograms per ml.

SUMMARY

Inhalation and nasal instillation of crystalline vitamin B_{12} in saline and lactose powder has produced satisfactory clinical and hematologic responses in six patients with pernicious anemia in relapse. Twenty patients with pernicious anemia in remission have been maintained by inhalation B_{12} techniques for over a period of one year.

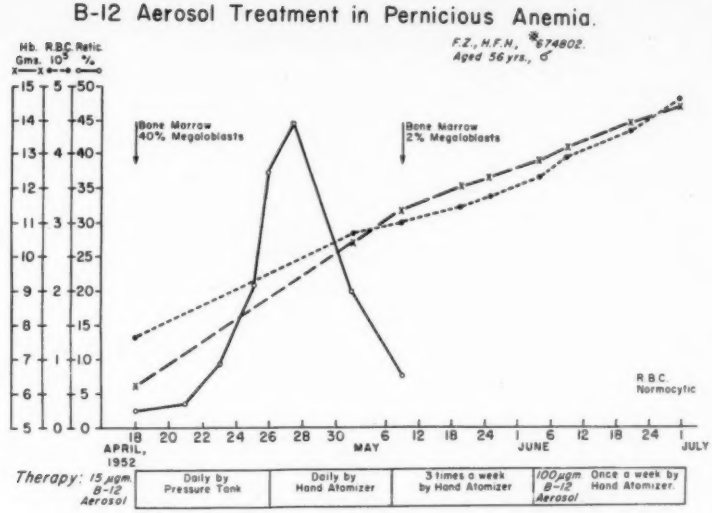


CHART 1

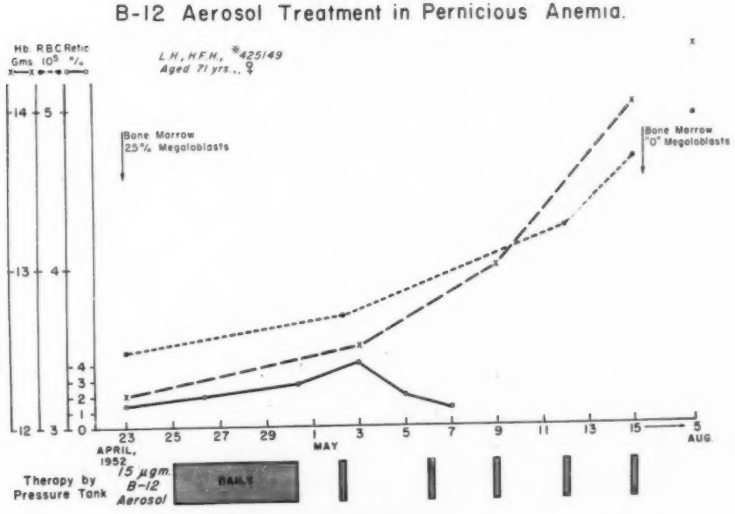


CHART 2

Charts 1, 2, 3 and Figure 1 with kind permission, from Monto, R. W., Rebuck, J. W., and Brennan, M. J.: Crystalline B_{12} Inhalation Therapy in Pernicious Anemia, AM. J. M. SC. Feb. 1953.

B-12 Dust Inhalation Treatment in Pernicious Anemia.

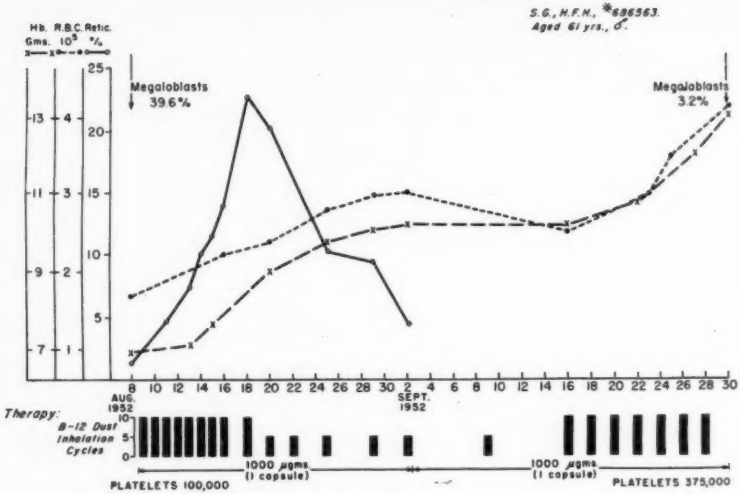
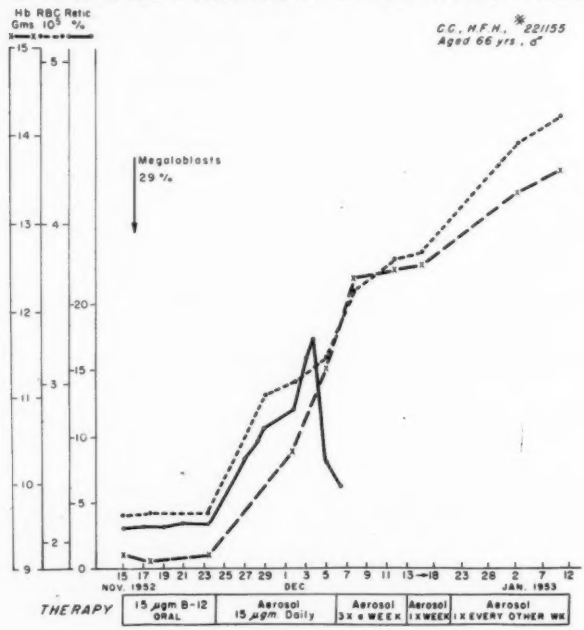


CHART 3

B-12 AEROSOL TREATMENT IN PERNICIOUS ANEMIA.



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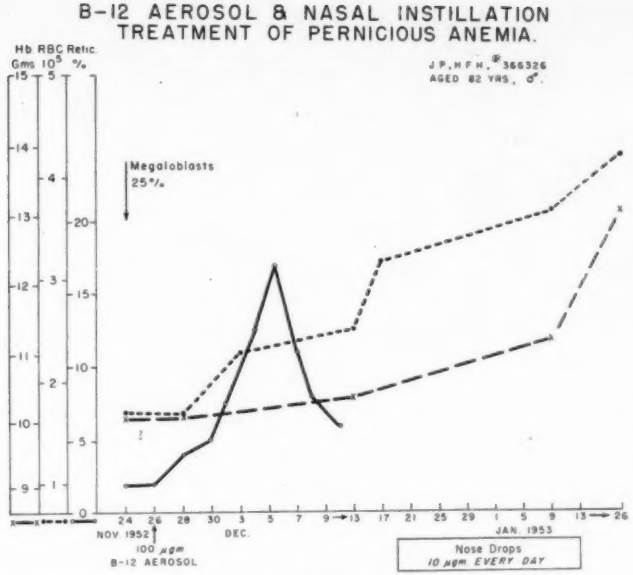

CHART 5

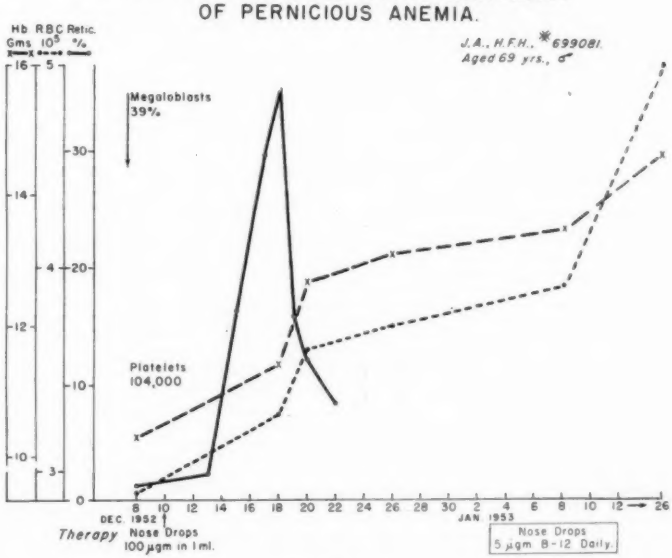

CHART 6

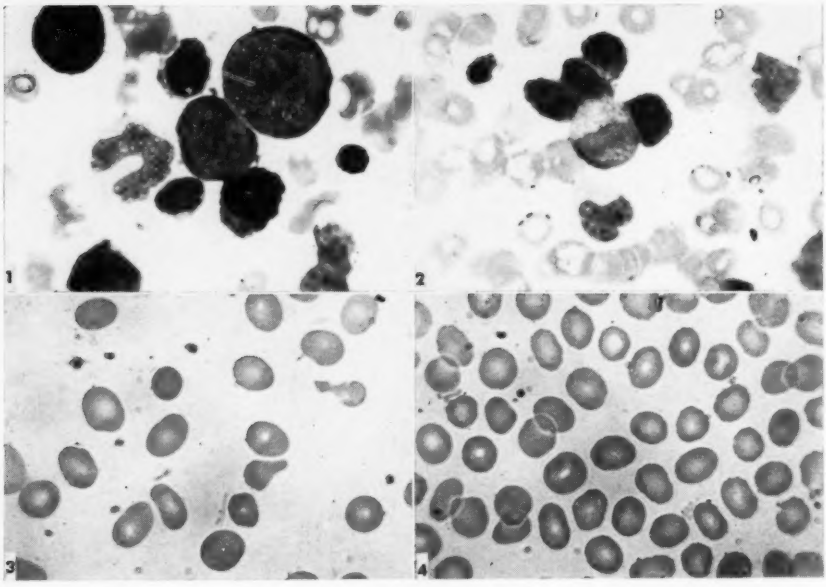

Figure 1

Fig. 1. Case 1. Representative megaloblasts and a giant neutrophilic metamyelecyte in the marrow aspirate prior to treatment. X1200.

Fig. 2. Case 1. Normoblasts and unaffected members of the neutrophilic series in the marrow aspirate after crystalline B_{12} aerosol treatment. X1200.

Fig. 3. Case 1. Megalocytes and poikilocytes in the peripheral blood prior to treatment. X1200.

Fig. 4. Case 1. Normocytes with only an occasional macrocyte in the peripheral blood after crystalline B_{12} aerosol treatment. X1200.

ACKNOWLEDGMENT

The authors wish to express appreciation to H. W. Schoenlein, Director of Bacteriological Laboratories, Difco Laboratories Incorporated, for supplying the crystalline B_{12}-lactose powder and the urinary B_{12} determinations.

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HETEROPIC PANCREATIC TISSUE IN THE GASTRIC WALL

ROBERT J. PRIEST, M.D.*

In 1859 Klob first identified heterotopic pancreatic tissue. This ectopic tissue has been found in all portions of the gastrointestinal tract and in adjacent organs. In an excellent review in 1950, Busard and Walters (1) tabulated 149 cases of heterotopic pancreatic tissue in the gastric wall. Since their review there have been 13 additional cases recorded in the literature (2,3,4,5,6,7,8). The following case presented the typical x-ray appearance of this lesion and offered perplexing symptoms mimicking peptic ulcer.

CASE REPORT

J.B.K., a 29 year old, white male, boiler fireman was seen in the Henry Ford Hospital gastro-intestinal clinic on September 19th, 1949. He complained of symptoms of one month's duration with a fluttering feeling in the abdomen, a constant hunger sensation in the epigastrium, and gnawing dull distress when the stomach was empty. The distress was completely, but temporarily, relieved by eating food or by taking baking soda. He had night distress, but no pain radiating to the back.

Physical examination revealed weight of 135 pounds, height of 70 inches. Eyes, ears, nose and throat were normal. There was no thyroid enlargement or lymphadenopathy. The chest was clear. The heart was not enlarged, no murmurs, or irregularities. The blood pressure was 115/60. The abdomen presented no palpable masses or tenderness. Genitalia and rectal examinations were normal.

Laboratory: The blood count and urinalysis were normal. Serology was negative. Fractional gastric analysis revealed a fasting free acid of 12 degrees, and a top free acid of 24 degrees after stimulating test meal.

X-ray of the chest was normal. An x-ray of the stomach was normal except that the duodenal cap filled with difficulty and a persistent defect with incisura was noted. In six hours the stomach emptied normally. X-ray of the colon revealed non-rotation of the cecum with the appendix lying in the upper right quadrant of the abdomen (see fig. 1).

The patient was placed on a strict ulcer management regime. He remained free from symptoms for three months. After an episode of nervous tension at his job, the typical ulcer rhythm returned. He had epigastric distress, relieved by eating. There was some pain at night. Progress x-ray of the stomach and duodenum in six months was similar to the first examination. Seven months later

*Associate in the Division of Gastroenterology.

he witnessed an attack of syncope in a neighbor. The epigastric burning distress returned and persisted for a week. During this recurrence a third x-ray of the stomach revealed a polypoid filling defect with smooth outline on the greater curvature of the pyloric antrum (see fig 1). In the center of the polypoid filling

Figure 1

Above: Note small fleck of retained barium in center of the defect.
Below, left: Smooth contour of filling defect on greater curvature near the pylorous.
Below, right: Non-rotation of the cecum with appendix in upper right quadrant.

defect there was retained a small fleck of barium. The lesion was found on fluoroscopy to be well fixed in this location. There was no delay in emptying the stomach.

Gastroscopy was done and the pylorous was observed to open and close, with shortening of the distal stomach. Slightly below the angulus on the greater curvature wall was observed a raised area at the convergence of several gastric rugal folds. This lesion did not appear to be a typical gastric polyp. The possibility of an intramural lesion was considered.

The patient was operated and the stomach palpated. A button-like, freely movable, small tumor was felt 2 cm. in diameter, and extending from a point 2.5 cm. proximal to the pyloric region. This was believed to be a benign lesion. Therefore a conservative resection of the distal stomach was performed at the junction of the lower and middle thirds of the stomach with anastomosis to the duodenum. The duodenum itself was normal to inspection and palpation. Vagotomy was not done. The appendix was removed because of its abnormal location and malrotation of the cecum.

The gross specimen presented a small raised area of mucosa near the pyloric end of the resected stomach. It was a well circumscribed submucosal mass. At

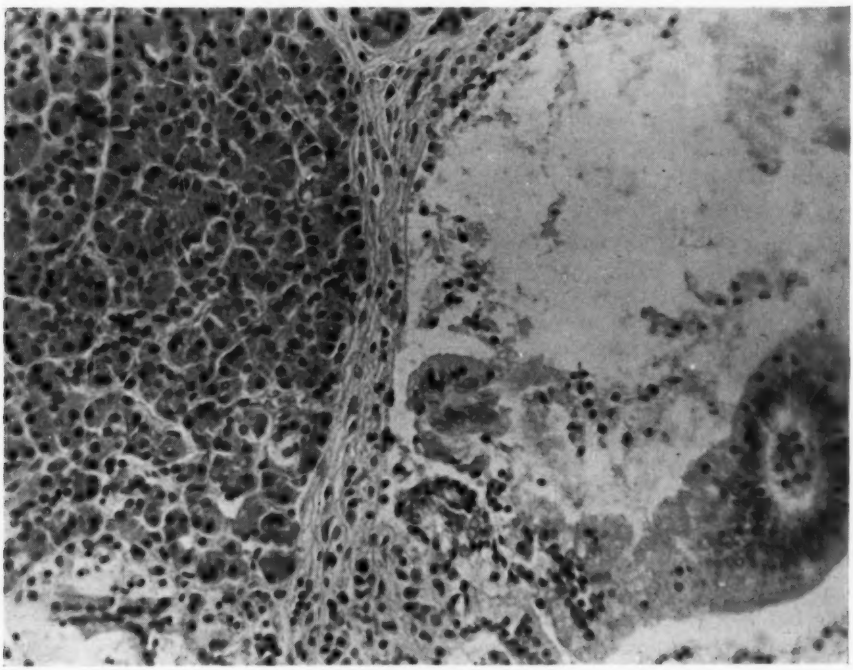

Figure 2

Pancreatic acini and ducts within the gastric mucosa and muscle.

its apex the mucosa was dimpled and appeared to have a pseudo-ostium. In cut section the mass was grayish white in appearance.

Microscopic examination of the tumor revealed a gastric mucosa without significant alteration. Within the mucosa, and more marked within the muscle, were numerous islands of pancreatic acini and ducts (see fig. 2). The ducts were lined by orderly epithelium, surrounded by well formed stroma, containing a very slight infiltrate of chronic inflammatory cells. There were no islets of Langerhans identified.

The patient recovered promptly from the operative procedure and has remained symptom free for eighteen months.

COMMENT

Cases of heterotopic pancreatic tissue in the stomach are not rare. They offer a challenge in diagnosis to the roentgenologist and to the surgeon. Their recognition as benign tumors is important, if unduly radical gastric surgery is to be avoided. Several authors have drawn attention to the wisdom of a more conservative operative procedure than subtotal gastrectomy (6,8,13,15).

The aberrant pancreatic tissue in the stomach may be subject to all the complications which affect the pancreas proper. Thus hemorrhage, carcinoma, and necrosis have been described. Jacobs (5) has considered those cases in which the heterotopic pancreatic tissue causes an ulcer-like syndrome, as perhaps the most perplexing. Many cases have been reported with symptoms similar to peptic ulcer (1,2,3,4,5,6,7,8,9,11,12,13). Symptoms may also be suggestive of pyloric obstruction, cholecystitis, or malignant gastric neoplasm. Pancreatic rests may be found in the presence of histamine-refractory achlorhydria (14).

Benner (6) and Littner (8) have recently emphasized the gross appearance of these lesions as a guide to their recognition during surgery. The gross morphology has been described in the literature, as a mucosal nodule like a nipple (7), a pedicle (11), a papillary projection (2), umbilicated (10), mucosal diverticulum (1), or the summit of lesion notched (9). Benner preferred to call the mucosal depression a pseudodiverticulum. The heterotopic pancreatic tissue is usually a relatively firm mass in the submucosa. Overlying is the moundlike mucosa, at the apex of which is a centrally located pit or pouch.

The roentgen appearance of this mucosal dimple has been described by Kjellman (3,4) and Littner (8). When a barium fleck is caught in the dimple of the pseudodiverticulum, the finding is highly suggestive of heterotopic pancreatic tissue. The smooth filling defect of this lesion is usually less than 2-4 cm. in diameter and is located in the antrum. Differentiation from leiomyoma may be difficult; the latter is usually much larger. Many reported cases have had normal x-ray studies of the stomach and duodenum, prior to the definitive x-ray which demonstrated the filling defect of this lesion. Jacobs (5) reported a case similar to the one presented here, in which a deformed and irregular duodenal bulb was found to be entirely normal at laparotomy.

The explanation for symptoms mimicking peptic ulcer has been attributed by Waugh and Harding (13) to various factors: (a) pyloric obstruction with polypoid excrescence into the lumen, (b) although no organic stenosis, the presence of the tissue in the muscular wall may interfere with peristaltic activity, (c) peptic ulceration may actually arise from the discharge of pancreatic juice through a duct into the submucosa.

SUMMARY

A case is presented of heterotopic pancreatic tissue in the gastric antrum. This condition gave symptoms simulating peptic ulcer. Surgery verified the tumor, but not the ulcer.

The gross appearance of the lesion with dimpled mucosa and a pseudodiverticulum, enabled the surgeon to select less radical surgery for this benign lesion. When present, the x-ray finding of a fleck of barium in the central depression of the polypoid defect may help in the differential diagnosis.

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RADIOACTIVE IODINE I 131 IN THE HENRY FORD HOSPITAL

JOHN H. L. WATSON, Ph.D.*

Radioactive Iodine is an isotope of ordinary iodine with identical properties, including those of metabolic nature, except that it is an unstable atom which breaks down with release of gamma and beta radiations. Its half-life is 8 days. It is made by deuteron bombardment of tellurium in a cyclotron; or in a chain-reacting uranium pile, both by neutron bombardment of tellurium and as a fission product of U 235.

As might be expected, it is widely used in thyroid studies, both as a therapeutic and as a tracer or diagnostic tool. As a therapeutic agent it is used to treat hyperthyroidism and carcinoma of the thyroid, and to relieve symptoms of Angina Pectoris in selected cases. As a tracer material it is used to estimate the thyroid's ability to pick up the element, and to determine the location of the gland or of "hot" nodules within it.

Shipments of I 131 are received twice a month by the Physics Laboratories of the Edsel B. Ford Institute for Medical Research from the Atomic Energy Commission works at Oak Ridge, Tennessee, and are available to all departments of the Hospital for human and/or animal application. Requests for material are made on the forms provided by the local Isotope Committee, through its Secretary, Doctor C. M. McColl.

Two services are offered for *tracer* studies in Hospital patients. The first of these is an I.P.D. procedure in which the patient is admitted to a room on B-4 and remains in the Hospital for two or three days. A tracer dose of 50 microcuries is given orally and both uptake and excretion data are collected. The patient is scanned thoroughly for uptake on four occasions during the period, at approximately 4, 24, 28, and 48 hours. At 24 hours a percentage uptake by the whole glandular area is determined by a phantom technique developed in this laboratory.** At the same time, and often for longer periods, urines are collected and the volumes and times of voidings are noted. Aliquots from each urination are sent to the radioactive laboratories for determinations of activity. From these data the relationship between cumulative percent of I 131 excreted is plotted against time. The slope and quantitative data of these graphs are significant as regards the ability of the thyroid to pick up iodine. From them it is possible to decide whether the patient retains iodine in a manner characteristic of hyper - eu - or hypothyroidism. In addition, the slope of such a curve yields information on

*Chief of the Physics Department, Edsel B. Ford Institute for Medical Research.

**L. E. Preuss, "A Simple Radioactive-Thyroid Phantom" *Nucleonics*, Vol. 9, No. 4, p. 72-74, (October, 1951).

renal efficiency. A report on these studies, with suggestions for dosage if the patient requires therapeutic treatment, are prepared and sent to the doctor who requested the dose. The tracer is a diagnostic tool in real or supposed thyroid disorders and an indicator of foci of thyroid activity.

The second tracer service is executed more briefly in the O. P. D. It is a less expensive, less time consuming procedure which involves only uptake scanning. The scanning is done over only a few selected areas and the service is applicable only to patients for whom a simple decision is required as to whether the patient retains iodine in an abnormal or normal manner. The service is handled from the Emergency desk in the M-Unit Arcade. Again, a report is sent to the referring doctor.

The use of radioiodine therapeutically presupposes that an I.P.D. tracer study has been carried out from which some accurate estimation of dosage has been possible. The dose is prepared in the radioactive laboratory and sent to the referring doctor's office for oral administration. In therapy, the patient must be followed carefully clinically and the dosage repeated until the desired results are achieved. Symptoms of thyroiditis must be looked for, and remembering that the therapy is the equivalent of a total or partial thyroidectomy, symptoms of thyroid storm must also be expected when hyperthyroid patients are treated.

Radioiodine therapy of hyperthyroidism is indicated whenever the patient is a poor risk for operation or when surgery is refused. Radioiodine therapy of thyroid carcinoma is always indicated, with surgery or without it. With carcinoma the dosage is large (about 25 MC) and is repeated every two weeks for periods of months. The iodine radiation should be applied ideally before any x-ray is given. In selected cased, radioiodine therapy is the treatment of choice to relieve symptoms of Angina Pectoris.

I 131 is given only to patients who have satisfied certain preliminary dietary requirements. Particular among these is that they receive no iodine or thyroid medication for a period of four weeks prior to the dose. If this is not done, the possibility exists of chemical blockage of the relatively small amounts of I 131.

A summary of present clinical uses to which I 131 is being put in the Hospital follows:

1. Diagnostic in thyroid disorders (adult).
2. Therapy in hyperthyroidism.
3. Therapy for carcinoma of the thyroid and its metastases.
4. Therapy for angina pectoris in selected cases, with concurrent tracer studies.

Clinical Research Projects being conducted in collaboration with the Physics Department personnel include:

1. "A Study of I 131 as a Diagnostic Tool in Children Suspected of Thyroid Disorders," with Dr. J. A. Johnston of the Pediatrics Department.

2. "A Study of Total Thyroidectomy Patients Using I 131, in Order to Follow Thyroid Metabolism in Such Patients," with Dr. D. E. Szilagyi of General Surgery. This is a continuing research. The I 131 tracer methods were used by Dr. Szilagyi to assist in problems on the effects of adrenocortical stimulation on thyroid function. The same procedures are being used in studies on the survival of thyroid autotransplants.

3. The researches begun on the use of I 131 labelled diiodofluorescein in the localization of brain tumors have been discontinued but the project is still open for reinstatement with the Department of Neurosurgery.

4. Analysis of I 131 tracer data (1) with relation to its use in diagnosing kidney failure and particularly in investigating certain diuretic effects, and (2) with relation to devising a means of determining quantitatively from the data (a) rate of excretion of I 131; (b) rate of thyroid uptake of I 131; and (c) the disappearance rate of the I 131.

Two papers only have been published from the Hospital on experimental results with I 131 although many papers have been published with reference to Radioisotopes in general. The two papers published are:

1. D. Emerick Szilagyi, M.D., Arthur B. McGraw, M.D., and Nicholas P.D. D. Smith, M.B., B.Ch., M.Sc. (Dublin) "The Effects of Adrenocortical Stimulation on Thyroid Function," *Ann. Surg.*, *136*, 555 (1952).

2. D. Emerick Szilagyi, M.D., Roy D. McClure, M.D., Thomas H. Connell, Jr., M.D., John H. L. Watson, Ph.D., and Luther E. Preuss, M.S., "Radioiodine (I 131) Tracer Studies After Total Thyroidectomy," *Ann. Surg.*, *134*, 546-565, (October, 1951).

Several papers have been read before national meetings by Doctor Szilagyi and his staff on results of these studies.

During 1952 a total of 135 separate doses of radioiodine were prepared and delivered by Physics for clinical studies. Among the departments of the Hospital, these were distributed as: General Medicine, 15; General Surgery, 62; Cardio-Respiratory, 24; Pediatrics, 15; Metabolism, 9; Infectious Diseases, 6; Endocrinology, 2; and Cancer Clinic, 2. No other departments asked for service. At the same time 47 doses of P 32 were delivered (45 to General Medicine and 2 to Ophthalmology) and 3 shipments of radioactive gold colloid were received, one for General Medicine and two for Gynecology and Obstetrics. The application of radioisotopes, and especially of Iodine (I 131), is growing wider in the Hospital and with the O.P.D. service operating should increase even more during 1953.

ACUTE BARBITURAL INTOXICATION

HOWARD R. MARVEL, M.D.*

Barbituric acid derivations are the most popular and widely used drugs of the sedative and hypnotic group. They are easily available and do not come under the stringent regulations of the Harrison Narcotic Act. In fact only twenty-seven states have laws preventing their sale without prescription by a physician. As a result accidental and deliberate intoxications are common. In the last ten years there has been a remarkable increase in the number of cases of barbiturate intoxication arriving at large city hospital emergency rooms. A review of the subject of acute barbiturate intoxication is appropriate to all of us who must treat these emergencies as they arrive.

Although there are numerous barbiturate preparations on the market, only a few are of major importance. In terms of duration of action these are:

Long duration	*Moderate duration*	*Short duration*
Phenobarbital	Amytal	Seconal
Barbital	Pentobarbital	

An ultra-short actor, sodium pentothal, actually a thiobarbiturate, while commonly used in anesthesia, is not generally used with suicidal intent.

Barbital and phenobarbital are just as capable of producing coma as the shorter acting drugs. Their absorption from the gastro intestinal tract is somewhat slower but their elimination from the body is also much slower. Traces of barbital may be found in the urine nine days after a hypnotic dose. Eight per cent of the drug will be excreted in twelve hours, twenty per cent in twenty-four hours and thirty-five to sixty-five per cent in forty-eight hours. The slow rate of excretion is the basis for the cumulative effects of the long actors. In the presence of kidney damage the excretion rate may be even slower.

The moderate and short acting barbiturates are detoxified by the liver. Their action may be prolonged and more profound in cases where severe liver impairment is present.

The lethal dose of the various barbiturate preparations for human beings can not, of course, be definitely established. The presence or absence of kidney or liver disease as well as the general health must be considered in evaluating the prognosis of a given case. The reader is referred to the recent publications of Koppanyi and Fazekas[1] for further information regarding lethal dosage.

The diagnosis of acute barbiturate intoxication is usually simple. The great majority of patients who attempt suicide will tell relatives or friends what they

*Associate in Medical Clinic Number 4, Department of Medicine.

have done or will admit taking the drug on direct questioning before they lapse into coma. Frequently, an empty medicine bottle will be noted near the patient. In some instances, however, a patient in a stuporous state may take repeated doses without realizing what he is doing. Rarely the ingestion may be accidental or may occur in a concealed form with homicidal intent.

The signs and symptoms vary. In the beginning there is dullness in the head, muscular incoordination and impairment of smell and taste. Later there is dysphagia, occasionally nausea and vomiting, stupor, sleep and coma. Occasionally excitement and hallucinations occur before stupor and sleep overcome the patient. The patient in coma progresses on to shallow respirations and circulatory collapse. Death may be due to circulatory collapse, bronchial pneumonia or respiratory failure.

The diagnosis should always be suspected in the comatose patient who is breathing quietly and regularly. Laboratory tests are slow and tedious and, therefore, do not have much practical value. They are, however, of medico-legal importance.

Considerable controversy exists in respect to the various methods of treatment available for the patient. Treatment possibilities vary from the symptomatic therapy proposed by Nilsson[2] on to the various stimulants and analeptics and finally to electrostimulation.

Koppanyi[1] believes that prognosis based on tables of degrees of coma is not reliable. He believes that all cases in coma should receive an orientation dose of metrazol, (5cc of a ten per cent solution intravenously). If a favorable response occurs, only symptomatic care is indicated. A favorable response consists of coordinated voluntary movement, a return of corneal reflexes, an increase in muscle tone and improvement in circulatory status. If the response is favorable then metrazol, 5cc every ten to fifteen minutes until complete awakening, is used. If the response is unfavorable picrotoxin is used. The initial dose is twenty-five milligrams intravaneously, then fifteen milligrams every fifteen minutes until there is evidence of awakening, or at least a return of reflexes. The dose is then reduced but not discontinued until the patient can perform voluntary purposeful movements.

Reed, Driggs, and Foote,[3] after experiences with 300 cases, have proposed the following system of classification of coma.

Group 0—A patient who is asleep but can be roused and will sit up in bed, drink fluids, etc.

Group 1—A patient who is comatose but will withdraw from painful stimuli such as venipuncture, slapping, pinching, etc. There is no circulatory embarrassment and all reflexes are intact.

Group 2—A patient who does not withdraw from painful stimuli but has no respiratory or circulatory depression and, most important of all, whose reflexes are intact.

Group 3—A patient whose reflexes are mostly or entirely gone but who shows no evidence of respiratory or circulatory depression.

Group 4—A patient with absent reflexes, respiratory depression with cyanosis, or circulatory failure and shock, or both.

The authors emphasize that grouping should not be done until an airway is established. They also consider the tendon reflexes most reliable and have found pupil size and corneal reflexes unreliable criteria in many instances.

Analeptic drugs are then used according to the grouping as follows:

Group 0 to 1—observation, no analeptics.

Group 2—Caffeine and sodium benzoate 0.5 gram every two hours. Do not exceed six grams in twenty-four hours; or amphetamine twenty-five milligrams every two hours but not over three hundred milligrams in twenty-four hours.

Group 3—Caffeine or amphetamine as above, if reflexes not restored in fifteen to twenty minutes give picrotoxin every fifteen to twenty minutes intravenously. Use 1cc (three milligrams); if no twitching give a second dose of six milligrams and watch, continue as necessary until twitching occurs.

Group 4—Caffeine or amphetamine as before, then if necessary picrotoxin six to nine milligrams every twenty minutes. A Drinker respirator should be used if necessary. Oxygen should be used but with great care because the anoxic stimulus on the carotid body is the only mechanism left for maintaining respiration.

Most authors[3, 6] agree as to the symptomatic measures necessary for satisfactory care of the patient. They are:

1. Careful observation—blood pressure, pulse, respirations, and reflexes every half hour. Observation is of the greatest importance because the degree of coma may change and the plan of therapy may need to be altered.

2. Immediately on arrival an adequate airway should be established. If laryngospasm is present an endotracheal tube should be inserted. Bronchoscopy should be done if aspiration of vomitus occurs.

3. Place bed in the shock position and turn the patient frequently.

4. Prophylactic antibiotics; penicillin, usually, but in the presence of shock and hypostatic pneumonia broad spectrum antibiotics may be more effective.

5. In all patients except those in extremis, do gastric lavage. This is important because a portion of the drug may lie dormant in the stomach, in deep coma and later be absorbed as recovery begins.

6. Fluid balance as in any unconscious patient.

7. Ninety-five per cent O_2, five per cent CO_2—with care when the patient is in deep coma.

8. Observation for cardiac arrhythmias. This is especially important in patients receiving caffeine or amphetamine. The dose limits proposed by Reed, et al, should not be exceeded.

9. Treatment of circulatory collapse may require the use of pressoramines in the event that the other symptomatic measures, oxygen and analeptics, do not restore the blood pressure.

Nikethamide and disodium succinate have not been found to be effective. Electrostimulation[4, 5] has been reported as a successful mode of therapy in a few cases but further results must be reported before final evaluation can be made.

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NEPHRECTOMY FOR TUBERCULOSIS. REVIEW OF 96 CASES

JOHN K. ORMOND, M.D.* and
RICHARD C. SLOCUM, M.D.**

From 1916 to 1950 a period of thirty-five years, ninety-six patients have undergone nephrectomy for renal tuberculosis at the Henry Ford Hospital. This represents seventeen per cent of all nephrectomies performed during this time.

Many advances have been made in the treatment and early diagnosis of pulmonary tuberculosis and a decline noted in the incidence of all forms of extrapulmonary tuberculosis. For this reason it is perhaps interesting to compare nephrectomies for tuberculosis with nephrectomies for other causes during successive five year periods. (Table 1.) Males and females were represented almost equally, 47 males and 49 females.

TABLE 1—COMPARISON—5 YEAR PERIODS

Year	*Nephr. Tb.*	*Nephr. Other*	*Per Cent*
1916–20	3	8	27
1921–25	4	48	7
1926–30	25	50	33
1931–35	18	58	23
1936–40	13	71	15
1941–45	17	106	13
1946–50	16	128	11

TABLE 2—AGE INCIDENCE

	Number of Cases	*Per Cent*
1–10	1	1
11–20	4	4.1
21–30	20	20.8
31–40	39	40.6
41–50	23	23.9
51–60	6	6.2
61–70	—	—
71–80	—	—

The age incidence showed that the greatest number of patients were in the fourth decade. (Table 2.) The youngest was a boy of seven and the oldest fifty-nine.

*Formerly Chief of the Division of Genito Urinary Surgery. Now teaching in Miraj Medical Center at Miraj, India.

**Senior Resident in the Division of Genito Urinary Surgery.

In the vast majority of these patients there was evidence of involvement of only the kidney that was removed. The other kidney showing no pus and no pyelographic evidence of destruction. In very few a tuberculous pyonephrosis was removed even though pus cells and tubercle bacilli were found in the urine from the opposite kidney.

The usual operative procedure was simple nephrectomy with excision of as much ureter as possible. Complete nephroureterectomy was performed in twenty-seven cases in which there was evidence of lower ureteral involvement.

There were four operative deaths, with an operative mortality rate of 4.1 per cent.

A brief review of these deaths is presented:

Henry Ford Hospital No. 77219—expired during the immediate postoperative period of uncontrollable hemorrhage.

Henry Ford Hospital No. 373944—expired on the eighth postoperative day of tuberculous meningitis.

Henry Ford Hospital No. 434096—expired on the twentieth postoperative day with tuberculous peritonitis, a duodenal fistula and thrombosis of the vena cava and renal vein.

Henry Ford Hospital No. 149377—this patient had an incision and drainage of a perinephric abscess one month prior to nephrectomy. Death occurred one day following nephrectomy. Post mortem examination revealed bilaterial destruction of the adrenal corices.

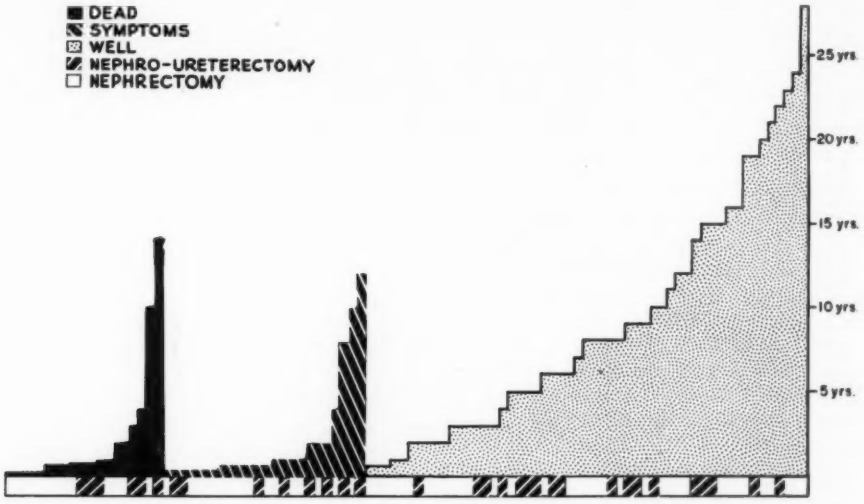
Nineteen of the patients operated on had either a wound infection or wound separation with persistent sinus formation. Only thirteen patients received streptomycin during the operative period but none of these had a wound infection or sinus formation.

Three patients, one of whom was mentioned among the operative deaths, had adrenal cortical destruction. Two of these were diagnosed clinically as Addisons disease and all were confirmed at autopsy.

Fifteen or thirty-two per cent of the male patients had associated genital tuberculosis as evidenced by nodularity of the vas, epididymis or prostate. Thirty-six patients presented evidence of extra-genital tuberculosis, usually pulmonary or bone and joint.

The average duration of cystitis among those who recovered was a little less than a year. In four patients symptoms of cystitis and continued infection persisted until death fourteen, ten, four and three years after surgery. Three patients still living have continued to have pyuria and symptoms of cystitis intermittently for twelve, ten and eight years.

Of the ninety-six patients fourteen were operated on within the past five years and are omitted from the statistics concerning survival. Twenty-four patients were lost to follow up during the first five years following nephrectomy. Nineteen patients are known to have died. Thirty-nine patients were known to be alive for at least five years following nephrectomy and have been followed an average of 12.2 years. In computing the five year survival, the twenty-four patients lost to follow up have been added to the known deaths giving the maximum possible deaths as forty-three. This results in a 47.5 per cent minimum five year survival. Excluding those lost to follow up the five year survival is sixty-seven per cent.



Graph Depicting Results and Follow-up of the Ninety-six Patients Undergoing Nephrectomy for Tuberculosis.

AUTHOR'S BOOK REVIEW. ELECTRO CARDIOGRAPHIC STUDIES IN NORMAL INFANTS AND CHILDREN

ROBERT F. ZIEGLER, M.D.*

The work reported in this monograph was done with the single purpose of defining accurately the characteristics of the electrocardiogram in normal infants and children. The ultimate purpose to be served will, of course, be a more accurate means of determining abnormal variations for use in clinical pediatric cardiology.

The book may be divided into four major sections. The first (Chapt. I) is a review of the literature, which has reference value but little practical worth. The second, (Chapts. II thru VIII) provides the textual material—a description of materials and methods, and a presentation of the age sequence of practically every electrocardiographic measurement. The third section (Chapt. IX) consists of an atlas of representative electrocardiograms in normal children from birth to the age of 16 years. The fourth (Appendix) is a graphic presentation of statistical data from which the likelihood of any electrocardiographic measurement being normal or abnormal may be determined.

Although little is included concerning basic electrocardiographic principles, thereby making the book of small value to a beginner, a graphic basis is laid for determining from the precordial leads the normal progression of relative right and left ventricular mass. This, of course, provides a sound basis for the detection at any age of abnormal ventricular size, and is of interest to pediatric cardiologists as an important diagnostic help. Many other types of normal data are presented, from which valuable studies of abnormal data should be forthcoming.

This book obviously represents a great deal of work on what might at first glance be considered a very small subject. The subject is not really so small, however, since it represents not only a specific cardiological problem but also one that is basic to the entire subject of electrocardiography.

No review would be complete without adding that the publishers have done a magnificent job of preparing this book. The illustrations have been beautifully reproduced, and the format if not the material makes it very readable.

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*Associate in Cardiology in charge of Section of Pediatric Cardiology, Henry Ford Hospital, Detroit.
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